REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

Summary of Status of Amendments and Office Action

In the present amendment, claims 55-78 are added and claims 1-54 are canceled. Therefore, claims 55-78 are pending in the application, with claims 55, 61, 67, and 73 being independent. Applicants have re-ordered the subject matter recited in claims 33-54, now canceled, and re-present them in new claims 55-78.

Independent claims 55, 61, 67, and 73 correspond to previous independent claims 33-36, respectively, and also recite language from previous dependent claims 46-51. That is, independent claims 55, 61, 67, and 73 each recites the same language of independent claims 33-36, but also now each further recites "and wherein the active peptide is selected from human growth hormone and human insulin." Applicants reserve the right to pursue canceled subject matter in a continuation application.

Applicants have amended the claims to more clearly recite the claimed subject matter, and to provide claims presented in proper dependent order. Support for the amendments is found in the application as filed. Applicants also note that new claims 55-78 recite the same claim language previously presented and considered by the Office in claims 33-42, 46-51, and 52-54, now all canceled. No new matter is added.

Notice of Allowance Vacated

Applicants have been advised that the Notice of Allowance mailed June 11, 2003, by Examiner Arun Chakrabarti has been vacated. The present Office Action was mailed March 23, 2005 by Examiner Bradley L. Sisson. Applicants appreciate the Office's acknowledgement that the issue fee payment of September 5, 2003, may be refunded, credited to a deposit account, or applied to the subsequent issue fee when this case is found to be allowable.

Claim Objections

The Office Action objects to the format of the claims because claims that depend from a dependent claim should not be separated by any claim that does not also depend from said dependent claim. For example, claims 33-36 are independent claims which are followed by dependent claims that depend separately from claims 33, 34, 35, or 36. For the convenience of the Examiner, Applicants have amended the claims to present them in proper order of dependency, thereby rendering this objection moot.

Rejections Under 35 U.S.C. § 112, first paragraph

Written Description

Claims 33-54 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the claims contain subject matter that is not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. Specifically, the Examiner alleges that the specification fails provide "an adequate

written disclosure of the immense genus of proteins the claimed powders are to comprise."

In order to advance prosecution, and without acquiescence, Applicants have amended the independent claims to further recite "and wherein the active peptide is selected from human growth hormone and human insulin." Working examples of employing human growth hormone are described in the specification. As for human insulin, although a working example is not set forth in the specification for the peptide, it is a peptide and thus shares a common characteristic in chemical structure, i.e., both are made of peptide bonded amino acids, as noted in the specification (page 6, lines 18-21). Thus it is reasonable to think that the stabilization effect during peptide powder formation, which is confirmed with human growth hormone, will also be seen in human insulin.

Moreover, as for absorption of a peptide through mucous membranes, human insulin, consisting of 51 amino acids, is a much smaller peptide than human growth hormone (consisting of 191 amino acids in the case of 22 K hGH) as described in the specification (page 29, lines 2-4). Also, there is a further structural similarity between the two peptides in that they both have two intramolecular S-S bonds as noted in the specification (page 29, line 2-11). In addition, smaller peptides are generally more likely absorbed through mucous membranes as stated in the specification.

The Examiner asserts that the specification does not provide a definition of what "human insulin" is as compared to non-human insulin. Applicants submit that human insulin is a well known compound, and its entire chemical structure is well defined and well known to anyone skilled in the art at the time of filing. Therefore, anyone skilled in

the art at the time of filing would have directly known from the term "human insulin" the meaning and the scope of the compound thus referred to.

The Examiner also alleges that the specification does not provide adequate written description of the structure and function of human growth hormone. However, human growth hormone (22K and 20K, page 11, lines 19-25) is also well known to anyone skilled in the art. Anyone skilled in the art will directly know from the term "human growth hormone" the meaning and scope of the compound thus referred to. The term itself conveys the detailed identity of the peptide without requiring any additional information in the specification. So, one skilled in the art does not need any specific information be given in the specification of the structure or function of human growth hormone. Thus, an adequate written description is given to human growth hormone in the specification. And, since the identity of human growth hormone is conveyed to anyone skilled in the art, the specification provides an adequate written description for distinguishing human growth hormone from other growth hormones.

Given the facts described in the specification and in the drawing (page 28, lines 11-16, table 7, and Fig. 4) that human growth hormone was successfully administered transpulomonarily, it is quite reasonable to think that this will also be the case with human insulin. Thus, Applicants submit that the claimed subject matter is described in the specification and through the description in the specification it is clear to one skilled in the art that the Applicants had possession of the claimed invention at the time the application was filed.

Therefore, Applicants respectfully request that the written description rejection of claims 33-54, and as applied to new claims 55-78, under 35 U.S.C. § 112, first paragraph, be withdrawn.

Enablement

Claims 33-54 are rejected under 35 U.S.C. § 112, first paragraph, because the Examiner asserts that, as discussed above, the specification does not reasonably suggest that the Applicants were in possession of the invention at the time of filing, and that it is allegedly well settled that one cannot enable that which they do not possess. Accordingly, the Office states that the same deficient specification allegedly cannot and does not enable the making and use of these as yet unrealized and non-described peptide-containing powders. Applicants traverse the rejection for the reasons discussed above and for the following additional reasons.

However, in order to advance prosecution, and without acquiescence, Applicants have amended the independent claims to further recite "and wherein the active peptide is selected from human growth hormone and human insulin." As described above, the specification describes in detail processes for production of claimed powders employing human growth hormone. Thus, a person skilled in the art can readily make and use the present invention, now reciting human growth hormone. With regard to human insulin, the peptide shares a common characteristic (that it consists of peptide-bonded amino acids and includes two intramolecular S-S bonds) and has smaller molecular weight. So, anyone skilled in the art can readily carry out the invention (powder and inhalant composition) referring to the relevant description in the specification, with simple

replacement of a peptide from human growth hormone to human insulin. Even if some experimentation is needed, it must be just routine and supplementary experimentation. Therefore, undue experimentation is not required. The Federal Circuit has made this clear. In Enzo, the court noted that "we have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be 'undue'." *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 U.S.P.Q. 2d 1129 (Fed. Cir. 1999) Thus, the enablement requirement is met.

Therefore, Applicant's claims are enabled, and the rejection to claims 33-54, and as applied to claims 55-78, under 35 U.S.C. § 112, first paragraph should be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Rose, Patton, Okada

Claims 31-35, 37-39, 41-45, 52, and 53 are rejected under 35 U.S.C. § 103(a) over U.S. Patent 5,839,443 to Rose et al. ("Rose"), U.S. Patent 5,607,915 to Patton ("Patton-1"), and U.S. Patent 6,455,053 B1 to Okada et al. ("Okada").

To establish a prima facie case of obviousness, the combination of cited references with the knowledge generally available to one of ordinary skill in the art must teach or suggest all of the recited limitations of the claims. Also, the Office must demonstrate that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or combine reference teachings. In addition, the Office must demonstrate that there was a reasonable expectation of success. See MPEP 2143.

Furthermore, the teaching or suggestion to make the claimed modification must be found in the prior art, not in the Applicants' disclosure. See *In re Vaeck* , 947 F,2d 488, 20 USPQ 2d 1438 (fed Cir 1991). In the present case, the Office has failed to make a prima facie case of obviousness because it has not met any, let alone all of the above criteria.

First, Applicants note that they have amended all the independent claims to further recite "and wherein the active peptide is selected from human growth hormone and human insulin." Furthermore, the record does not indicate that the combination of references teach or suggest all of the recited limitations of the claimed powder wherein the active peptide is selected from human growth hormone and human insulin. Accordingly, for at least this reason, a prima facie case of obviousness has not been shown for this combination of cited references, and Applicants respectfully request reconsideration and withdrawal of this rejection.

Second, Applicants also traverse the rejection as the Office has not established a prima facie case of obviousness for the additional reason that there is no motivation in the cited documents for the ordinary skilled artisan to combine the documents at the time of filing to devise the claimed invention.

The suggestion to combine or modify the prior art teachings must be clear and particular. *See In re Dembiczak,* 175 F.3d 994, 999 (Fed. Cir. 1999). Thus, while a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the prior art, that modification is not obvious unless the prior art suggested the desirability of such a modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984). Furthermore, the Office has the burden to provide some objective evidence, not found in

the Applicants' specification, or reasoned argument showing that one of ordinary skill in the art would have been motivated to combine the prior art to devise the claimed invention. *In re Lee*, 277 F.3d 1338, 1433 (Fed. Cir. 2002).

Applicants submit that the Office has failed to establish a *prima facie* case of obviousness because there simply is no clear and particular suggestion in the cited references to combine the lyophilized physiologically active peptide composition of Rose with (1) Patton's lyophilized parathyroid hormone particles and with (2) Okada's solid preparations comprising 40% saccharide to devise the claimed powders.

Rose lists a variety of materials among which are Pluronic F68, mannitol, polyvinyl alcohol, polyvinylpyrrolidone. However, the Office admits that Rose does not disclose any specific example employing mannitol. Patton-1 also does not provide any example combination containing mannitol. Okada's preparations are solid ones, like a tablet, and are not powder. Okada teaches that 40% content of saccharide is preferred for rapid dissolving preparations. Mannitol is included in saccharide in Okada, therefore no description is given therein to a combination of mannitol and a peptide, much less any relative quantity of a peptide and mannitol.

Therefore, Okada does not teach or suggest any combination of mannitol and a peptide. And as Okada is addressed to solid preparations (like tablets), without any specific example of peptide-containing preparations, let alone preparations containing human growth hormone or human insulin, there must be no motivation to combine Okada with Rose or Patton-1.

Motivation to devise the claimed invention at the time of filing is found only in Applicants' specification. As there is no motivation for the Okada, Rose, and Patton-1

combination to devise the compositions claimed, this rejection should be withdrawn, for this additional reason, as being an improper combination rejection.

Therefore, the Examiner has not met the burden of showing a prima facie case of obviousness. For at least these reasons, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §103(a).

Rose, Patton-1, Okada, Harris, Patton-2

Claims 43-51 are rejected under 35 U.S.C. § 103(a) over Rose, Patton-1, and Okada as applied above and further in view of U.S. Patent 5,334,162 to Harris ("Harris"), and U.S. Patent 5,997,848 to Patton et al. ("Patton-2").

Applicants traverse the rejection as the Office has not established a prima facie case of obviousness for the same reasons discussed above that there is no motivation in the cited documents for the ordinary skilled artisan to combine the documents at the time of filing to devise the claimed invention. The further combination of the previous references with Harris and Patton-2 does not correct this deficiency.

Harris merely discloses a lyophilized growth hormone preparation containing cartridge assembly. No information is obtained from Harris regarding components of the growth hormone preparation, such as relative amount of mannitol to peptide, a binder, or a nonionic surfactant. Patton-2 describes insulin-containing lyophilized composition for respiratory delivery of insulin and states that particles having a diameter less than 10μm are preferred. However, no description is given to relative amount of mannitol to peptide, a binder, or a nonionic surfactant. Therefore, Harris and Patton-2 adds no additional information to what is disclosed by Rose, Patton-1, and Okada.

In view of the above, Applicants contend that the Office has merely identified a combination that might be feasible, but has not proffered clear and particular evidence concerning the desirability of combining Rose's lyophilized physiologically active peptide composition with Patton-1's lyophilized parathyroid hormone particles with Okada's solid preparations comprising 40% saccharide with Harris's lyophilized growth hormone preparation containing cartridge assembly and with Patton-2's lyophilized insulin preparation. Moreover, "a general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). At best, it may have been obvious to try such a combination. However, obvious to try is not the standard. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988); M.P.E.P. § 2145(X)(B).

The Office's broad conclusory statement regarding the obviousness of Rose's composition with the general formulation disclosures of Patton-1, Okada, Harris, and Patton-2 to devise a powder that would have a size suitable for use in inhalation therapy, and also have exhibited improved solubility is not based upon objective evidence of record or a reasoned argument as is required by *In re Lee*. The mere fact that references can be combined does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Here, Applicants submit that the cited references do not suggest the desirability of combining the lyophilized compositions of Rose, Patton-1, Harris, and Patton-2 with the solid preparations of Okada. The only motivation to combine the references and derive the claimed invention comes from the Applicants' own specification.

Applicants respectfully request that the Office reconsider and withdraw the rejection.

Rose, Patton, Okada, Ecanow, Oyama

Claims 36 and 40 are rejected under 35 U.S.C. § 103(a) over Rose, Patton-1, and Okada as applied above and further in view of U.S. Patent 4,963,367 to Ecanow ("Ecanow"), and U.S. Patent 6,117,434 to Oyama et al. ("Oyama").

Applicants traverse the rejection as the Office has not established a prima facie case of obviousness for the same reasons discussed above that there is no motivation in the cited documents for the ordinary skilled artisan to combine the documents at the time of filing to devise the claimed invention. The further combination of the previous references with Ecanow and Oyama does not correct this deficiency.

Ecanow generally discloses physiologically-active compounds encapsulated by an aqueous coacervate-based film or matrix for use in inhalation. The Office cites Ecanow for disclosing use of lecithin for drug delivery. Oyama discloses humectant compositions useful for cosmetics and external preparations. The Office cites Oyama for disclosing hydrogenated lecithin as allegedly enhancing solubility.

Applicants submit that one of ordinary skill in the art would not be motivated to combine the cited references with Ecanow's physiologically-active compounds encapsulated by an aqueous coacervate-based film or matrix with the other cited references to devise a powder comprising lecithin, mannitol, and a peptide. Neither would one of ordinary skill in the art be motivated combine the cited references with Oyama's use of hydrogenated lecithin to enhance solubility of humectant compositions

useful for cosmetics and external preparations to devise a powder comprising hydrogenated lecithin, mannitol, and a peptide. It is not readily obvious to combine components of a humectant composition useful for cosmetics and external preparations to select components to modify a physiologically active powder, such as is disclosed by Rose.

Applicants incorporate by reference herein the above arguments in regards to Rose, Patton-1, and Okada and why a prima facie case of obviousness has not been met. Further, Applicants submit that the further combination with Ecanow and Oyama does not correct the deficiencies.

The mere fact that references can be combined does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Here, Applicants submit that the cited references do not suggest the desirability of combining the lyophilized compositions of Rose, Patton-1, Harris, and Patton-2 with the individual lecithin component selected from Ecanow's physiologically-active compositions encapsulated by an aqueous coacervate-based film or matrix, or hydrogenated lecithin component selected from Oyama's humectant compositions useful for cosmetics and external preparations. The only motivation to combine the references and derive the claimed invention comes from the Applicants' own specification.

Applicants respectfully request that the Office reconsider and withdraw the rejection.

CONCLUSION

For the foregoing reasons, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested.

If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
Yoshinobu HANYU et al.

Bruce H. Bernstein
Reg. No. 29,027

Stephen M. Roylance
Reg. No. 31,296

Monday, July 25, 2005
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191